Citation:

Little RE, Anderson KW, Ervin CH, Worthington-Roberts B, Clarren SK. Maternal alcohol use during breast-feeding and infant mental and motor development at one year. *N Engl J Med*. 1989; 321(7):425-30.

PubMed ID: 2761576

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

The aim of this study was to determine if an infant's mental and motor development at age one is related to the infant's exposure to alcohol in the breast milk during the first three months postpartum.

Inclusion Criteria:

- Pregnant women members of the Group Health Cooperative of Puget Sound, a health maintenance organization
- Obtained prenatal care during the period from May 1982 through August 1983
- Informed consent was obtained
- Cohort groups were formed with the goal of 200 women in each
    - Women who breastfed their infants for more three months and were classified as "heavier" drinkers during postpartum (absolute alcohol score of ≥1.0 or report of binge drinking)
    - Women who breastfed their infants for more three months and were classified as "lighter" drinkers during postpartum (all other mothers, including nondrinkers)
    - Women who breastfed their infants for less than one month and were classified as "heavier" drinkers during postpartum (absolute alcohol score of ≥1.0 or report of binge drinking)
    - Women who breastfed their infants for less than one month and were classified as "lighter" drinkers during postpartum (all other mothers, including nondrinkers)

Exclusion Criteria:

- Men and non-pregnant women
- Pregnant women receiving prenatal care before May 1982 or after August 1983
- Women who had not obtained prenatal care by the sixth month of gestation

Description of Study Protocol:

Recruitment

- Pregnant women of the Group Health Cooperative of Puget Sound completed a screening questionnaire with information on her diet, drinking, smoking and intentions with respect to breastfeeding in the sixth month of her pregnancy
- The subjects were selected from this pool to meet the goal of 200 women per study group

Design

- Prospective Cohort Study

Blinding used

- The assessments of the infants were conducted by clinicians with no knowledge of the mothers' characteristics

Intervention

- Two personal interviews were conducted with the women after the first and third months postpartum to assess information on alcohol intake and breastfeeding practices
- Infant's development was measured wtih the Bayley Scales of Infant Development at age one

Statistical Analysis

- Differences between the two groups of infants with respect to demographic characteristics and life style of the mother were evaluated by the chi-square test or the t-test
- Regression analysis was performed on the more than 100 independent variables
- Any variable identified as potentially confounding was included in the final regression analysis
- Subjects with extreme values were omitted and the analyses were redone
- Considered statistically significant if P value ≤ 0.05

Data Collection Summary:

Timing of Measurements

- Personal interviews were completed after the first and third postpartum months
    - Information was obtained on diet, drinking, smoking and other drug use since the initial screening
    - Four-day food records for the mother and baby were completed
    - Additional four-day food records for the mother and baby were completed after the second postpartum month
- Developmental assessment was completed within two weeks of the infant's first birthday

Dependent Variables

- Bayley Scales of Infant Development
    - Mental Development Index
    - Psychomotor Development Index

Independent Variables

- Infant's exposure to ethanol in the postpartum period
  - Maternal absolute alcohol (AA) score was determined
    - Estimate of the average number of ounces of ethanol ingested daily
    - An AA score of 1.0 reflects an average daily consumption of 29.6 ml (1 oz) of ethanol, about two standard drinks
  - Number of binges
    - Consumption on a single occasion of 74 ml (2.5 oz) or more of ethanol, about five standard drinks
  - Infant's exposure to ethanol was determined
    - The mother's AA score was weighed for each month by the proportion of days in that month during which she breastfed the infant and averaging the values obtained for the three-month period

Control Variables

- Rate of smoking (number of cigarettes smoked daily)
- Marijuana use
- Amount of caffeine consumed
- Intake of nutrients
  - Average daily kilocalorie, protein and 14 selected micronutrients were calculated
  - Nutrients were converted to a percentage of the Recommended Dietary Allowance

Description of Actual Data Sample:

Initial N: 4,262 women were screened

Attrition (final N):

- "Heavier" drinkers (mothers with an AA score of ≥1.0 or a report of binge drinking): 153
- "Lighter" drinkers (all other mothers including nondrinkers): 247
  - Proportion of long-term and short-term breastfeeding were kept comparable in both drinking groups
- Only 153 women who reported heavier drinker had infants who passed their first birthday and had the development test completed, therefore the number of mothers in the lighter drinking cohort was increased to maintain a total number of 400 women
- One infant could not complete the PDI part of the developmental test

Age:

- Infants with AA scores <0.5
  - <20 years: 6.4%
  - 20-29 years: 55.2%
  - 30-39 years: 37.1%
  - ≥40 years: 1.3%
  - Mean age: 28
- Infants with AA scores ≥0.5
  - <20 years: 0%
  - 20-29 years: 35.6%
  - 30-39 years: 64.4%
  - ≥40 years: 0%

- Mean age: 31

Ethnicity:

- Infants with AA scores <0.5
  - White: 94.6%
  - Nonwhite: 5.4%
- Infants with AA scores ≥0.5
  - White: 96%
  - Nonwhite: 4%

Other relevant demographics:

Characteristic	Infant AA Score	
	<0.5	≥0.5
	Percent or mean	
Martial Status		
Married	85.3	97
Not married	14.7	3
Years of School		
<12	5.7	0
12-15	64.2	41.6
≥16	30.1	58.4
Mean number of years	14	16
Family Income		
<$10,000	8.3	2
$10,000-$25,000	43.1	35.7
≥$25,000	48.6	62.2
Nutrient intake (mean % of RDA)		
Kilocalories	85	92
Total protein	145	147
Micronutrients	68	72
Mean months of breastfeeding in year after delivery	6	9

Drug use between delivery and third interview		
Mean maternal AA score	0.2	0.9
Binge drinking	24	49
Cigarette smoking	38	26
Marijuana use	19	26
High caffeine use	26	37

Location: Seattle, Washington

Summary of Results:

Key Findings

- The linear trend was significant (P=0.006) for the Psychomotor Development Index (PDI) scores of infants according to the Infant AA score
  - PDI of infants with an Infant AA Score of ≥1.5 was 85±11.1 and average PDI for all infants was 102±19.1
  - Linear trend persisted even when the four infants with Infant AA Scores ≥1.5 were excluded (P=0.028)
- The mothers of the infants exposed more heavily to alcohol were older, better educated, more likely to be married, higher family income, higher nutrient intake, more likely to use marijuana and have high caffeine intakes than the mothers of the infants with less exposure
- The association between infant's PDI score and the Infant AA score persisted even after tobacco, marijuana and caffeine intake were controlled for
- Regression analysis of the PDI score, the Infant AA score and maternal age indicated a decrease of 7.5 points in the PDI
  - Translates to a mother having an average of two drinks daily in the three months after delivery and breastfeeding exclusively without supplementing, the infant's PDI would be predicted to decrease by 7.5 points.

Other Findings

Mean Mental Development Index (MDI) and Psychomotor Development index (PDI), According to the Infant AA Score and the Duration of Breastfeeding in Infants with AA Scores below 0.5

Infant AA Score And Duration of Breastfeeding	Number of Infants	MDI	Number of Infants	PDI

0.0	111	105±14.3	111	104±18.7
Short-term	79	106±14.4	79	105±17.3
Long-term	32	105±14.4	32	103±22
>0.0-0.4	188	105±14	188	103±19.4
Short-term	51	101±15.6	51	103±21.1
Long-term	137	107±13.1	137	103±18.8
0.5-0.9	71	105±17	71	99±19.1
1.0-1.4	26	109±15.2	25	98±18.1
≥1.5	4	108±10.5	4	85±11.1
All infants	400	106±14.7	399	102±19.1
Linear Trend Significance		NS		0.006

All infants with AA scores ≥0.5 had mothers who were long-term breastfeeders, except one infant with an infant AA score in the 0.5-0.9 range. This infant had a MDI of 109 and a PDI of 122.

Mean MDI and PDI, According to the Infant AA Score and the Level of Maternal Drinking during Pregnancy and Postpartum

Period and Infant AA Score	**Lighter Drinking**		**Heavier Drinking**	
	Number of Infants	MDI	Number of Infants	MDI
Pregnancy				
0.0	90	106	21	101
>0.0-0.4	147	105	39	106
0.5-0.9	45	104	26	106
1.0-1.4	19	108	7	113
≥1.5	3	103	1	122
P Value	NS		0.03	
Postpartum				
0.0	82	104	29	108
>0.0-0.4	140	105	48	106
0.5-0.9	25	103	46	106
1.0-1.4	0	-	26	109

≥1.5	0	-	4	108
P Value	NS		NS	
Pregnancy				
0.0	90	105	21	102
>0.0-0.4	147	102	39	106
0.5-0.9	45	96	26	104
1.0-1.4	18	98	7	98
≥1.5	3	85	1	86
P Value	0.003		NS	
Postpartum				
0.0	82	104	29	106
>0.0-0.4	140	101	48	108
0.5-0.9	25	97	46	99
1.0-1.4	0	-	25	98
≥1.5	0	-	4	85
P Value	NS		0.007	

Mean MDI and PDI, According to the Infant AA Score (AA) for all Infants and for Those Born to Nonusers of Selected Drugs

Group of Infants	**AA <0.5**			**AA ≥0.5**			
	Number	MDI	PDI	Number	MDI	PDI	Significance
All infants	299	105	103	101	106	98	P<0.01
With no exposure through breast milk							
To alcohol consumed in binges	258	105	103	52	105	98	NS
To tobacco	222	105	104	75	105	96	P<0.001
To marijuana	258	105	103	75	104	97	P<0.05

To high caffeine levels	275	105	103	69	108	99	P<0.05
With no exposure during pregnancy							
To alcohol consumed in binges	239	106	103	73	105	95	P<0.01
To tobacco	178	105	103	66	104	96	P<0.01
To marijuana	243	105	103	80	104	98	P<0.05
To high caffeine levels	269	106	103	82	106	98	P<0.05

P values were determined by t-test of the mean PDI scores in the two groups of infants divided by infant AA score.

Change in MDI and PDI per Unit of Increase in the Infant AA Score and the Mother's Age, in the Infants of 247 Women with Consistent Lactation Status after Leaving the Hospital

Index	Infant AA Score	Mother's Age
MDI		
Change per unit of increase (95% CI)	1.0 (-3.6 to 5.6)	-0.4 (-0.8 to 0.0)
P Value	0.672	0.033
PDI		
Change per unit of increase (95% CI)	-7.5 (-13.3 to -1.7)	-0.5 (-1.0 to 0.0)
P Value	0.012	0.044

Includes all the women who did not breastfeed their infants after leaving the hospital and those who breastfed for three months postpartum, with no supplemental use of milk or formula.

The change in the MDI or PDI with a change in a given independent variable was the coefficient for that variable from the regression of the MDI or PDI on the infant's alcohol exposure and the mother's age. The amount of change shown assumes that other variables were held constant.

Total R^2=0.019; overall F=2.301 (df=2,244); P=0.102

Total R^2=0.052; overall F=6.747 (df=2,244); P=0.001

Author Conclusion:

Infant's motor development at age one was significantly lower in infants who were regularly exposed to alcohol during lactation. The difference persisted even after controlling for more than 100 potential confounding variables. There was no association with maternal alcohol use and infants' mental development.

Reviewer Comments:

The sample is very homogenous, consisting mostly of white, well-educated, middle class women. There is the potential for mis-reporting of alcohol intake.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes

2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	No
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	Yes
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes

5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	Yes
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	Yes
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	Yes
6.6.	Were extra or unplanned treatments described?	Yes
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes

	7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**		Yes
	8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes